Analyst

PERSPECTIVE

View Article Online
View Journal | View Issue

Cite this: *Analyst*, 2025, **150**, 3237

The international society for clinical spectroscopy; reflections on the first 10 years

Małgorzata Baranska, [a] Hugh J. Byrne, [b] Peter Gardner, *[c,d] Alex Henderson, [e] Nick Stone [f] and Bayden Wood [g]

Received 11th April 2025,
Accepted 13th June 2025

DOI: 10.1039/d5an00419e

rsc.li/analyst

The article provides a perspective overview of the development and current status of the field of biomedical spectroscopy, on the occasion of the tenth anniversary of the foundation of the International Society for Clinical Spectroscopy (CLIRSPEC). It provides a background into the prior evolution of the field, and international community, and rationale for the foundation of the legal entity, CLIRSPEC. It describes the continued dissemination and educational activities associated with the society, and maps out key technical developments, as well as trends towards clinical translation, and future perspectives.

Background

2025 marks the 10th anniversary of the formal establishment of the International Society for Clinical Spectroscopy (CLIRSPEC)[1] as a Private Company Limited by Guarantee on the Registrar of Companies for England and Wales on 30th June 2015. The venture was progressed through the UK Engineering and Physical Science Research Council (EPSRC) Clinical Infrared and Raman Spectroscopy for Medical Diagnosis Network (also CLIRSPEC, 2014–2017). As an international society, CLIRSPEC is a non-profit organisation, with a stated objective to act as a platform for those individuals, teams and organisations wishing to promote the translation of spectroscopy into the clinical environment, for the general benefit of patients; for example, to improve patient diagnosis and prognosis. The Memorandum of Association of the society[2] also includes aspirations to;

- Promote a broader representation (*e.g.* of gender and nationality) of individuals working within the field of clinical spectroscopy;
- Organise national and international public lectures, meetings, debates and conferences;
- Engage in outreach activities of all sorts;
- Participate in, support, fund and disseminate research, innovation and other activities relating to the objectives;
- Award scholarships and bursaries raised from third party contributions to enable attendance at, and travel to, any national or international congresses related to the (society)

In reality, the measure was deemed necessary to protect the interests of the growing clinical spectroscopy community, largely academic based, which had evolved through a series of conference events, and national and international collaborative networks, largely based on the drive of individuals, who were subjected to increasing burden of workload and financial commitment.

Historical perspectives

The historical development of vibrational spectroscopy, and specifically biological applications, has been reviewed by Henry Mantsch, one of the early pioneers of the field.[3,4] Beginning in 1997, the so-called Berlin IR workshop,[5] hosted by Dieter Naumann and Peter Lasch at the Robert Koch Institute, was initially targeted at IR spectroscopic analysis of pathogens and microorganisms, but laterally expanding to include vibrational spectroscopy, and clinical applications more broadly, did much to crystallise and sustain a kernel of the vibrational spectroscopy community, particularly in Europe. The first SPEC Conference in Winnipeg (2000) has also been flagged as a key milestone. Under the tagline of "Shedding new light on disease", the event precipitated the biennial series of conferences which was continued through similar events in Reims (2002), Newark (2004), Heidelberg

[a]*Department of Chemical Physics, Faculty of Chemistry, Jagiellonian University, Gronostajowa 2, 30-387 Krakow, Poland*
[b]*Physical to Life Sciences Research Hub, FOCAS, City Campus, Technological University Dublin, Dublin 8, Ireland*
[c]*Photon Science Institute, University of Manchester, Oxford Road, Manchester, M13 9PL, UK. E-mail: peter.gardner@manchester.ac.uk*
[d]*Department of Chemical Engineering, School of Engineering, University of Manchester, Oxford Road, Manchester, M13 9PL, UK*
[e]*Manchester Institute of Biotechnology, University of Manchester, Princess Street, Manchester, M1 7DN, UK*
[f]*Department of Physics and Astronomy, University of Exeter, Exeter EX4 4QL, UK*
[g]*School of Chemistry, Monash University, Wellington Road, Clayton, VIC 3800, Australia*

(2006), São José dos Campos (2008), Manchester (2010), Chiang Mai (2012), Kraków (2014), Montreal (2016), Glasgow (2018), Monterey (2020 cancelled due to COVID-19), Dublin (2022) and most recently in Ioannina (2024). Starting in 2010, the proceedings of the conferences have been published through special issues of Analyst.[6–11]

A significant impetus, particularly in Europe, was the EU FP6 Special Support Action (SSA) Diagnostic Applications of Synchrotron Infrared Microscopy (DASIM–2005–2008) which, although targeted towards specific aspects of the field, included, for example a Raman Working Group, and clinical stakeholders and international advisors, and thus brought together key players in biological applications of vibrational spectroscopy through a targeted programme to identify key challenges. Although the programme did not fund research *per se*, the collaborative effort led to, for example significant developments in understanding and alleviating artefacts in both IR[12–14] and Raman[15–17] microspectroscopy. Above all, DASIM provided a platform for the emerging biospectroscopy community to begin to explore and establish consensus options on aspects of sample processing and presentation, instrument calibration, data preprocessing and analysis. As a deliverable of the SSA, the multi-author DASIM Book sought to provide a practical approach to biomedical applications of spectroscopy, from a clinical perspective.[18]

Efforts to maintain the momentum of the community consolidated by DASIM in Europe through applications to Marie Curie (now Marie Skłodowska-Curie) Training Networks and COST Actions were unsuccessful, and any collaborations were maintained largely on an informal, individual basis. In 2013, the UK EPSRC funded the national network, CLIRSPEC (2014–2017), bringing together expertise and stakeholders from the academic, clinical and instrumental manufacturers sectors across the UK, with international advisors. In addition to facilitating short term interlaboratory research exchanges, the network held two very successful conferences, in Exeter (2015) and Manchester (2017), and coordinated the Faraday Discussions meeting "Advanced Vibrational Spectroscopy for Biomedical Applications" in Cambridge, 2016.[19] As an integral part of its mission in training and development of early stage researchers, the Network instigated the CLIRSPEC Windermere Summer School in 2015, which continues to run annually, now under the umbrella of the CLIRSPEC International Society.

The legal foundation of the International Society CLIRSPEC was funded as an exit strategy of the UK EPSRC Network, and, as it was officially founded in June 2015, the two versions of CLIRSPEC overlapped until 2017, providing continuity. During this time, the activities also interacted strongly with those of the EU COST Action Raman4Clinics (2015–2018), which, amongst other outputs, produced two large-scale interlaboratory trials assessing the reproducibility of Raman[20] and surface enhanced[21] Raman.

The International Society adopted the SPEC series of conferences as its flagship, and, although the initial announcement of the impending foundation of the society was made at SPEC 2014 (Krakow), official association of the SPEC began with SPEC 2016 (Montreal), continuing with SPEC 2018 (Glasgow), SPEC 2020 (Monterey – cancelled due to COVID), SPEC 2022 (Dublin) and SPEC 2024 (Ioannina). Over the past ten years, the society has also expanded its dissemination brief to encompass association with a range of other conference and workshop series;

In November of 2017, CLIRSPEC became a member of the Federation of Applied Chemical and Spectroscopy Societies (FACSS – **https://facss.org/**), and thus has been formally represented in the annual SciX (**https://facss.org/scix-annual-conference**) programme since then.

In August 2019, CLIRSPEC teamed up with the Japan Association of Medical Spectroscopy (**https://medical-spectroscopy.jp/**) to support the CLIRSPEC Summer School in ASIA, in Kobe City (**https://sci-tech.ksc.kwansei.ac.jp/clirspecss/**).

In October 2019, CLIRSPEC became co-organiser of the 12th annual Workshop on "FT-IR Spectroscopy in Microbiological and Medical Diagnostics" hosted by the Robert Koch-Institute, Berlin, Germany.

CLIRSPEC was also an official organiser of the 11th (online-2021) and 12th (Kraków-2023) editions of the International Conference on Advanced Vibrational Spectroscopy (ICAVS).

In April 2021, the UK EPSRC accepted the proposal for the Grand Challenges in Healthcare Network, "Integrating Clinical Infrared and Raman Spectroscopy with digital pathology and AI: CLIRPath-AI" (**https://clirpath-ai.org/**). In terms of spectroscopic expertise, the network is an evolution of the UK EPSRC CLIRSPEC network, and has integrated the CLIRSPEC Windermere Summer School with a series of sandpit events exploring topics for short pump-prime projects, over the period 2021–2025, culminating in the final Network conference in May 2025.

Developments of state of the art

The evolution of the state of the art of clinical spectroscopy has previously been mapped out according to realms of clinical applications;[22,23]

1. *In vivo*;

a. Intraoperative characterisation of tumour resection margins

b. Endoscopic probes for disease detection

In both areas, the availability of near infrared optical fibre probes has favoured the use of Raman spectroscopy for *in vivo* applications, 1.a. having been demonstrated as early as 2010,[24–26] 1.b. in 2015.[27,28] The dominance of Raman in such applications has persisted, such that Raman probes for oesophageal cancer diagnosis are entering the stage of clinical trials,[29] and coherent Raman techniques have been increasingly explored.[30] A marked indication of progress towards clinical translation is the commercial development of both incoherent and coherent modalities for intra operative and endoscopic applications.[31–33]

2. *Ex vivo*;

a. Spectroscopic histopathology

The emergence of focal plane array technology meant that, by 2013, large scale (cm^2) biopsies could be screened using FTIR microscopy, albeit on timescales of >10 hours.[34] Progress was also made in the use of glass substrates which, although it limits the infrared spectral range, shows promise for simple tissue characterisation[35,36] and cellular analysis.[37,38] It has been demonstrated, however, that the full spectrum is not required to maintain diagnostic accuracy,[39] and the emergence of mid infrared tuneable quantum cascade laser systems prompted the exploration of discrete frequency IR imaging.[40,41] Further significant advances have been made through the use of deep learning methods, for example to reconstruct incomplete spatial domain IR data recording, which enables more rapid sample scanning.[42] Coherent Raman techniques have also been used for rapid histopathological screening, albeit also at discrete frequencies.[43] Ratios of Raman signals reflecting the relative lipid and protein contents can provide H&E like images, and convert the Stimulated Raman Scattering (SRS) signals into virtual H&E slides.[44] The Stimulated Raman Histology technique is now commercially available to image fresh tissue specimen without sectioning or staining, enabling near real-time histologic evaluation in the treatment room.[45]

b. Spectroscopic cytology

Although much of the pioneering work in spectrocytopathology was performed with IR absorption microscopy,[46,47] Raman microspectroscopy has become the more prominent choice for cytological applications in, for example cervical and oral cancer screening.[48–50] Hormonal effects,[51] blood contamination,[52] viral infection[53] and the influence of other confounding factors have been addressed, and protocols standardised to integrate as best as possible in the clinical workflow.[54] Process automation has been explored for high throughput screening,[55] and broadband CARS has been demonstrated for rapid classification based on individual cellular analysis.[56]

c. Liquid biopsies

An application which has seen particular growth over the past decade is that of diagnostic screening of liquid biopsies. The initial work, demonstrating the ability of ATR-FTIR spectroscopy of dried blood serum to distinguish between cancer *vs.* non-cancer, metastatic cancer *vs.* organ confined, brain cancer severity and organ of metastatic disease with high sensitivities and specificities,[57,58] has been progressed towards commercialisation,[59] as have the applications of Raman analysis of hydrated serum for colorectal cancers.[60] Of note also is the use of ATR-FTIR spectroscopy for the determination of malaria parasitaemia in whole blood samples, demonstrated in field trials in austere environments proving the robustness and capability of serum biofluid diagnostics.[61–63,64]

3. *In vitro*;

a. Drug screening and companion diagnostics

Applications of vibrational spectroscopy for *in vitro* screening of toxicants, including nanoparticulate materials,[65,66] chemotherapeutic agents,[67–69] radiation treatment,[70–72] stem cell differentiation[73] and virology,[74] have continued. Increasingly, attention has been devoted to kinetic studies of the cellular interactions, and subsequent cellular responses.[75–78] As the capabilities for analyses advance towards real-time, full spectral, subcellular visualisation of the cellular metabolism, the demands on the ability to data mine and interpret the responses also increases.[79–81]

In terms of clinical applications of vibrational spectroscopy, a somewhat overlooked area which has emerged over the past decade is that of analytical quality control in pharmaceutical dispensing,[82–85] and blood storage and transfusion.[86,87] Within the same time period, the world has seen an increasingly prominent usage of IR and Raman spectroscopies in security screening,[88] a development which may have a knock-on effect on clinical uptake.

b. Molecular diagnostics

Molecular diagnostics approaches are becoming increasingly important, particularly in the drive towards personalised medicine.[89] Although deep learning methods such as convolutional neural networks (CNN) are being increasingly used to analyse infrared and Raman spectra of biopsy tissue, they are often treated as a black box and it is difficult to associate specific spectral features with disease state.[90,91] This is a problem, since the European Union Artificial intelligence act deems the use of AI in medical diagnostics as high risk.[92] As a consequence, the act requires that the system must be sufficiently transparent to end users such as clinicians to enable them to understand, (i) how the AI works, (ii) what inputs it uses and most importantly in this context, (iii) the basis for its recommendations. This means that the AI has to be explainable, which, in most cases, means linking the spectral features to specific known molecular biomarkers. One example of this is the study by Goertzen *et al.* which showed that QCL data from lung cancer tissue could be linked with specific mutations (KRAS, EGFR, and TP53), with 95% sensitivity and specificity.[93] However, the concentration of most biomarkers is low and the signals are convoluted with the vast array of other constituent molecules, meaning that this is incredibly challenging.

A second approach to delivering explainability is to cross reference with other biological techniques. Linking IR spectral profiles of tissue to gene expression data is an emerging direction of research, linking spectral pathology with molecular biology. An example of this is the work by Tiwari *et al.*, who were able to link infrared data to a specific gene expression profile, referred to as ECM3 (Extracellular Matrix Cluster 3).[94] Another approach is to link spectral imaging data with mass spectrometry data, either using secondary ion mass spectroscopy (SIMS), matrix-assisted laser desorption/ionisation (MALDI) or proteomic analysis.[95–97] Correlating IR signatures with proteomic data has been shown to be particularly powerful and has led to the identification of a new biomarker for bladder cancer, specifically to differentiate urocystitis with reactive urothelial atypia and carcinoma *in situ* (CIS).[98]

An emerging area of research that could have an eventual impact in diagnosis is the characterisation of spectral signatures of kinetic processes at a cellular level. An example of this approach is the study of Goffin *et al.*, who applied a trajectory

inference analysis of the evolution of Raman spectroscopic profiles of the differentiation of adipocyte cells.[99] The application of cluster analysis enabled the identification and differentiation of the Raman spectral profiles of the different cell stages, which were then arranged in the sequence of the trajectory inference analysis. More recently, Kobayashi *et al.* demonstrated the prediction of single-cell RNA expression profiles in live cells by Raman spectroscopy.[100] Using the example of mouse stem cell differentiation, neural network prediction models were trained by correlating the Raman spectroscopic subcellular analysis profiles with corresponding single-molecule fluorescent *in situ* hybridisation (smFISH) profiles of nine anchor genes. These profiles were then correlated with those of the selected genes in single cell RNA sequencing analysis, enabling the evolution of the genomic profiles to be tracked in real-time, *in situ* in live cells, as they underwent the differentiation process. The analysis also yielded importance scores of the different features of the Raman spectra in predicting the cell-related marker genes, although the evolution of these features along the trajectory was not resolved. The use of deep learning techniques to associate label free spectroscopic "spectralomic" signatures with cellular events and/or processes may therefore open up avenues for a more holistic application of the techniques.[81]

4. Data processing and analysis;

Multivariate statistical analysis, including by machine and deep learning algorithms, continues to be the bedrock of clinical spectroscopy, and AI protocols for, for example, de-noising, and enhancing spatial resolution have emerged.[42,101–103] Multiblock and data fusion techniques are becoming increasingly explored, combining data from different techniques,[104] or biological samples.[105,106]

Sharing of datasets and analysis protocols has been high on the agenda of the society since its foundation. In addition to making data downloading, preprocessing and analysis scripts available through its Members' website,[1] the society established an open access Zenodo community.[107] Amongst the stated goals are to;

- Develop a standard data transfer format to allow free and easy dissemination of data between network members enhancing collaboration and efficiency of research funding
- Investigate the technological, cultural, ethical and IP issues in order to enable data sharing and reuse

In an effort to further embed the Findable, Accessible, Interoperable, and Reusable (FAIR) guiding principles for data management[108] in the biospectroscopy community, the FAIRSpectra initiative, launched in 2023 aims to; (i) develop an open file format for hyperspectral data produced by vibrational spectroscopies and mass spectrometries, and (ii) explore the metadata requirements for sharing such data.[109]

State of play and future perspectives

The past decade has been a period of rapid instrumental development, which continues to address limitations of spectroscopic sampling speed, spectral and spatial resolution, not just for short term clinical applications, but for more fundamental research, exploring the limits of label-free spectroscopic imaging and analysis. Coherent Raman Imaging is already integrated into established commercial optical microscopic platforms,[110] and commercial broadband systems are emerging.[111] QCL based IR microscopy is well established,[112,113] and the pulsed nature of the QCL systems has opened up a new field of hybrid techniques which provide IR absorption microspectroscopy with lateral resolution on the scale of tens of nanometers.[114,115] Of particular note are the photothermal systems, in which the IR absorption and Raman scattering spectra can be recorded from the same spot, with optical resolution (<1 μm), the newer models of which also integrate fluorescence microscopy.[116]

While the past decade has seen continued advancement of the spectroscopic and data analytical techniques available to the clinical spectroscopy community, a notable feature of that development is the emergence of commercial enterprises, either customising existing instrumentation,[59,60] or developing bespoke solutions for clinical applications.[31,33,45,117,118] These solutions are on the brink of realisation of clinical translation.[29,119,120]

As the efforts of the community to translate biospectroscopy into real clinical applications, a marked evolution has been that of the language used, which now includes aspects of clinical workflow and health economics,[121] patient perspectives,[122] and in turn reflects an increased awareness of the demands of the clinical sector. This has been developed through continued engagement with, and advocacy of, clinical practitioners.[123–125] In this context, the UK EPSRC Healthcare Technologies Grand Challenges network CLIRPath-AI specifically aims to synergistically combine expertise in clinical spectroscopy with that of Digital Pathology and Artificial Intelligence to progress and maximise the impact on healthcare. Accelerating the roll out of digital pathology for cancer screening in the National Health Service is high on the agenda of the UK Government,[126] and among the investments are the National Pathology Imaging Co-operative (NPIC), a centre of excellence in digital pathology and AI,[127] and the Pathology Image Data Lake for Analytics, Knowledge & Education (PathLake),[128] aiming to address the demand for AI-driven diagnostics to increase efficiency in pathology reporting and improve patient outcomes. Concerted engagement with such communities increases the visibility and profile of label free spectroscopic imaging for diagnostic applications, towards meaningful clinical translation.

Conflicts of interest

The authors of this paper are the current directors of the International Society for Clinical Spectroscopy.

Data availability

There is no data associated with this perspectives paper.

Acknowledgements

We would like to acknowledge former CLIRSPEC Directors Matthew Baker and Peter Lasch for their contribution to getting the society off the ground and also to EPSRC for the initial CLIRSPEC grant EP/L012952/1.

References

1 The International Society for Clinical Spectroscopy. Available from: **https://clirspec.org/** [cited 2025 Jan 25].
2 Memorandum and Articles of Association of the International Society for Clinical Spectroscopy, DOI: **10.5281/zenodo.15110006**.
3 H. H. Mantsch, The road to medical vibrational spectroscopy - A history, *Analyst*, 2013, **138**(14), 3863–3870, DOI: **10.3390/molecules26051439**.
4 H. H. Mantsch, Biomedical vibrational spectroscopy in the era of artificial intelligence, *Molecules*, 2021, **26**(5), 1439, DOI: **10.3390/molecules26051439**.
5 D. Naumann, FT-IR, spectroscopy of microorganisms at the Robert Koch Institute: experiences gained during a successful project, *Proc. SPIE*, 2008, **6853**(1), 68530G, DOI: **10.1117/12.761698**.
6 A. D. Meade, F. M. Lyng and H. J. Byrne, SPEC 2022: International Conference on Clinical Spectroscopy, *Analyst*, 2023, **148**, 6143, DOI: **https://doi.org/10.1039/D3AN90074F**.
7 P. Heraud and B. Wood, Editorial – the latest thinking and developments in optical diagnosis, *Analyst*, 2013, **138**(14), 3861–3862, DOI: **10.1039/C3AN90052E**.
8 M. Baranska and H. J. Byrne, Optical diagnostics – spectropathology for the next generation, *Analyst*, 2015, **140**(7), 2064–2065, DOI: **10.1039/C5AN90024G**.
9 K. M. Gough and F. Leblond, Optical diagnosis – highlighting the clinical applications of vibrational spectroscopy, *Analyst*, 2017, **142**(8), 1177–1178, DOI: **10.1039/C7AN90013A**.
10 M. Copsey, Encouraging collaboration in optical diagnostics, *Analyst*, 2015, **140**(7), 2064–2065, DOI: **10.1039/C005546H**.
11 M. J. Baker, SPEC 2018: International Society of Clinical Spectroscopy, *Analyst*, 2018, **143**(24), 5872–5873, DOI: **10.1039/C8AN90098A**.
12 P. Bassan, H. J. Byrne, J. Lee, F. Bonnier, C. Clarke, P. Dumas, E. Gazi, M. D. Brown, N. W. Clarke and P. Gardner, Reflection contributions to the dispersion artefact in FTIR spectra of single biological cells, *Analyst*, 2009, **134**(6), 1171–1175, DOI: **10.1039/B821349F**.
13 P. Bassan, H. J. Byrne, F. Bonnier, J. Lee, P. Dumas and P. Gardner, Resonant Mie scattering in infrared spectroscopy of biological materials - Understanding the 'dispersion artefact', *Analyst*, 2009, **134**(8), 1586–1593, DOI: **10.1039/B904808A**.
14 P. Bassan, A. Kohler, H. Martens, J. Lee, H. J. Byrne, P. Dumas, E. Gazi, M. Brown, N. Clarke and P. Gardner, Resonant Mie Scattering (RMieS) correction of infrared spectra from highly scattering biological samples, *Analyst*, 2010, **135**(2), 268–277, DOI: **10.1039/B921056C**.
15 L. M. Fullwood, G. Clemens, D. Griffiths, K. Ashton, T. P. Dawson, R. W. Lea, C. Davis, F. Bonnier, H. J. Byrne and P. Gardner, Investigating the use of Raman and immersion Raman spectroscopy for spectral histopathology of metastatic brain cancer and primary sites of origin, *Anal. Methods*, 2014, **6**(12), 3948–3961, DOI: **10.1039/C3AY42190B**.
16 F. Bonnier, A. Mehmood, P. Knief, A. D. Meade, W. Hornebeck, H. Lambkin, K. Flynn, V. McDonagh, C. Healy, T. C. Lee, F. M. Lyng and H. J. Byrne, In vitro analysis of immersed human tissues by Raman microspectroscopy, *J. Raman Spectrosc.*, 2011, **42**(5), 888–896, DOI: **10.1002/jrs.2825**.
17 F. Bonnier, S. M. Ali, P. Knief, H. Lambkin, K. Flynn, V. McDonagh, C. Healy, T. C. Lee, F. M. Lyng and H. J. Byrne, Analysis of human skin tissue by Raman microspectroscopy: Dealing with the background, *Vib. Spectrosc.*, 2012, **61**, 124–132, DOI: **10.1016/j.vibspec.2012.03.009**.
18 G. Williams, S. Fisher, J. Sule-Suso, J. M. Chalmers, G. Cinque and H. J. Byrne, *et al.*, *Biomedical Applications of Synchrotron Infrared Microspectroscopy*, in *Biomedical Applications of Synchrotron Infrared Microspectroscopy*, 2010, DOI: **10.1039/9781849731997**.
19 Advanced Vibrational Spectroscopy for Biomedical Applications: Faraday Discussion. Available from: **https://www.rsc.org/events/detail/16963/advanced-vibrational-spectroscopy-for-biomedical-applications-faraday-discussion** [cited 2024 Dec 23].
20 S. Fornasaro, F. Alsamad, M. Baia, L. A. E. Batista De Carvalho, C. Beleites, H. J. Byrne, *et al.*, Surface Enhanced Raman Spectroscopy for Quantitative Analysis: Results of a Large-Scale European Multi-Instrument Interlaboratory Study, *Anal. Chem.*, 2020, **92**(5), 4053–4064, DOI: **10.1021/acs.analchem.9b05658**.
21 S. Guo, C. Beleites, U. Neugebauer, S. Abalde-Cela, N. K. Afseth, F. Alsamad, *et al.*, Comparability of Raman Spectroscopic Configurations: A Large Scale Cross-Laboratory Study, *Anal. Chem.*, 2020, **92**(24), 15745–15756, DOI: **10.1021/acs.analchem.0c02696**.
22 H. J. Byrne, M. Baranska, G. J. Puppels, N. Stone, B. Wood, K. M. Gough, P. Lasch, P. Heraud, J. Sulé-Suso and G. D. Sockalingum, Spectropathology for the next generation: Quo vadis?, *Analyst*, 2015, **140**(7), 2066–2073, DOI: **10.1039/C4AN02036G**.
23 M. J. Baker, H. J. Byrne, J. Chalmers, P. Gardner, R. Goodacre, A. Henderson, S. G. Kazarian, F. L. Martin, J. Moger, N. Stone and J. Sulé-Suso, Clinical applications of infrared and Raman spectroscopy: State of play and future challenges, *Analyst*, 2018, **143**(8), 1735–1757, DOI: **10.1039/C7AN01871A**.

24 M. S. Bergholt, W. Zheng, K. Lin, Z. Huang, K. Y. Ho, K. G. Yeoh, M. Teh and J. B. Y. So, Characterizing variability in in vivo Raman spectra of different anatomical locations in the upper gastrointestinal tract toward cancer detection, *J. Biomed. Opt.*, 2011, **16**(3), 037003, DOI: 10.1117/1.3556723.

25 M. S. Bergholt, W. Zheng, K. Lin, K. Y. Ho, M. Teh, K. G. Yeoh, *et al.*, In vivo diagnosis of esophageal cancer using image-guided Raman endoscopy and biomolecular modeling, *Technol. Cancer Res. Treat.*, 2011, **10**(2), 103–112, DOI: 10.7785/tcrt.2012.500185.

26 Z. Huang, S. K. Teh, W. Zheng, K. Lin, K. Y. Ho, M. Teh and K. G. Yeoh, In vivo detection of epithelial neoplasia in the stomach using image-guided Raman endoscopy, *Biosens. Bioelectron.*, 2010, **26**(2), 383–389, DOI: 10.1016/j.bios.2010.07.125.

27 M. Jermyn, K. Mok, J. Mercier, J. Desroches, J. Pichette, K. Saint-Arnaud, *et al.*, Intraoperative brain cancer detection with Raman spectroscopy in humans, *Sci. Transl. Med.*, 2015, **7**, 274ra19, DOI: 10.1126/scitranslmed.aaa2384.

28 J. Desroches, M. Jermyn, K. Mok, C. Lemieux-Leduc, J. Mercier, K. St-Arnaud, K. Urmey, M.-C. Guiot, E. Marple, K. Petrecca and F. Leblond, Characterization of a Raman spectroscopy probe system for intraoperative brain tissue classification, *Biomed. Opt. Express*, 2015, **6**(7), 2380, DOI: 10.1364/BOE.6.002380.

29 Smart probe for oesophageal cancer diagnosis begins human trials – RaPIDE Diagnostics. Available from: https://rapide-diagnostics.co.uk/smart-probe-for-oesophageal-cancer-diagnosis-begins-human-trials/ [cited 2024 Dec 29].

30 M. Rodewald, H. Bae, S. Huschke, T. Meyer-Zedler, M. Schmitt, A. T. Press, *et al.*, In vivo coherent anti-Stokes Raman scattering microscopy reveals vitamin A distribution in the liver, *J. Biophotonics*, 2021, **14**, e202100040, DOI: 10.1002/jbio.202100040.

31 Our Optical Imaging Technology For Tumor Assessment | Reveal. Available from: https://revealsurgical.com/optical-imaging-technology/ [cited 2024 Dec 28].

32 Towards Spectrally Resolved Raman Endoscopy - Lightcore Technologies. Available from: https://lightcore-technologies.com/towards-spectrally-resolved-raman-endoscopy/ [cited 2024 Dec 28].

33 MarginGuide—RiverD. Available from: https://www.riverd.com/research-applications/marginguide/ [cited 2024 Dec 31].

34 P. Bassan, A. Sachdeva, J. H. Shanks, M. D. Brown, N. W. Clarke and P. Gardner, Whole organ cross-section chemical imaging using label-free mega-mosaic FTIR microscopy, *Analyst*, 2013, **138**(23), 7066–7069, DOI: 10.1039/C3AN01674A.

35 J. Tang, D. Kurfürstová and P. Gardner, Breast cancer detection using infrared spectral pathology from H&E stained tissue on glass slides, *Clin. Spectrosc.*, 2021, **3**, 100008, DOI: 10.1016/j.clispe.2021.100008.

36 M. J. Pilling, A. Henderson, J. H. Shanks, M. D. Brown, N. W. Clarke and P. Gardner, Infrared spectral histopathology using haematoxylin and eosin (H&E) stained glass slides: a major step forward towards clinical translation, *Analyst*, 2017, **142**(8), 1258–1268, DOI: 10.1039/C6AN02224C.

37 L. M. Dowling, P. Roach, A. V. Rutter, I. Yousef, S. Pillai, D. Latham, D. G. van Pittiius and J. Sulé-Suso, Optimization of Sample Preparation Using Glass Slides for Spectral Pathology, *Appl. Spectrosc.*, 2021, **75**(3), 343–350, DOI: 10.1177/0003702820945748.

38 A. V. Rutter, J. Crees, H. Wright, D. G. Van Pittius, I. Yousef and J. Sulé-Suso, Fourier transform infrared spectra of cells on glass coverslips. A further step in spectral pathology, *Analyst*, 2018, **143**(23), 5711–5717, DOI: 10.1039/C8AN01634H.

39 S. Mittal, T. P. Wrobel, L. S. Leslie, A. Kadjacsy-Balla and R. Bhargava, A four class model for digital breast histopathology using high-definition Fourier transform infrared (FT-IR) spectroscopic imaging, Proceedings of SPIE: Progress in Biomedical Optics and Imaging, 2016, Vol. 9791, pp. 310–317, DOI: 10.1117/12.2217358.

40 T. P. Wrobel and R. Bhargava, Infrared Spectroscopic Imaging Advances as an Analytical Technology for Biomedical Sciences, *Anal. Chem.*, 2018, **90**(3), 1444–1463, DOI: 10.1021/acs.analchem.7b05330.

41 M. J. Pilling, A. Henderson, B. Bird, M. D. Brown, N. W. Clarke and P. Gardner, High-throughput quantum cascade laser (QCL) spectral histopathology: a practical approach towards clinical translation, *Faraday Discuss.*, 2016, **187**, 135–154, DOI: 10.1039/C5FD00176E.

42 K. Falahkheirkhah, K. Yeh, S. Mittal, L. Pfister and R. Bhargava, Deep learning-based protocols to enhance infrared imaging systems, *Chemom. Intell. Lab. Syst.*, 2021, **217**, 104390, DOI: 10.1016/j.chemolab.2021.104390.

43 M. Ji, D. A. Orringer, C. W. Freudiger, S. Ramkissoon, X. Liu, D. Lau, *et al.*, Rapid, label-free detection of brain tumors with stimulated Raman scattering microscopy, *Sci. Transl. Med.*, 2013, **5**, 201, DOI: 10.1126/scitranslmed.3005954.

44 D. A. Orringer, B. Pandian, Y. S. Niknafs, T. C. Hollon, J. Boyle, S. Lewis, *et al.*, Rapid intraoperative histology of unprocessed surgical specimens via fibre-laser-based stimulated Raman scattering microscopy, *Nat. Biomed. Eng.*, 2017, **1**(2), 1–13, DOI: 10.1038/s41551-016-0027.

45 Stimulated Raman Histology | Invenio Imaging | Santa Clara. Available from: https://www.invenio-imaging.com/ [cited 2024 Dec 28].

46 J. M. Schubert, B. Bird, K. Papamarkakis, M. Miljković, K. Bedrossian, N. Laver, *et al.*, Spectral Cytopathology of Cervical Samples: Detecting Cellular Abnormalities in Cytologically Normal Cells, *Lab. Invest.*, 2010, **90**(7), 1068, DOI: 10.1038/labinvest.2010.72.

47 K. Papamarkakis, B. Bird, J. M. Schubert, M. Miljković, R. Wein, K. Bedrossian, *et al.*, Cytopathology by Optical Methods: Spectral Cytopathology of the Oral Mucosa, *Lab. Invest.*, 2010, **90**(4), 589, DOI: 10.1038/labinvest.2010.1.

48 F. M. Lyng, D. Traynor, I. R. M. Ramos, F. Bonnier and H. J. Byrne, Raman spectroscopy for screening and diagnosis of cervical cancer, *Anal. Bioanal. Chem.*, 2015, **407**, 8279–8289, DOI: 10.1007/s00216-015-8946-1.

49 I. R. Ramos, A. D. Meade, O. Ibrahim, H. J. Byrne, M. McMenamin, M. McKenna, A. Malkin and F. M. Lyng, Raman spectroscopy for cytopathology of exfoliated cervical cells, *Faraday Discuss.*, 2016, **187**, 187–198, DOI: 10.1039/C5FD00197H.

50 H. J. Byrne, I. Behl, G. Calado, O. Ibrahim, M. Toner, S. Galvin, C. M. Healy, S. Flint and F. M. Lyng, Biomedical applications of vibrational spectroscopy: Oral cancer diagnostics, *Spectrochim. Acta, Part A*, 2021, **252**, 119470, DOI: 10.1016/j.saa.2021.119470.

51 D. Traynor, P. Kearney, I. Ramos, C. M. Martin, J. J. O'Leary and F. M. Lyng, A study of hormonal effects in cervical smear samples using Raman spectroscopy, *J. Biophotonics*, 2018, **11**(6), e201700240, DOI: 10.1002/jbio.201700240.

52 D. Traynor, S. Duraipandian, C. M. Martin, J. J. O'Leary and F. M. Lyng, Improved removal of blood contamination from ThinPrep cervical cytology samples for Raman spectroscopic analysis, *J. Biomed. Opt.*, 2018, **23**(05), 055001, DOI: 10.1117/1.JBO.23.5.055001.

53 D. Traynor, C. M. Martin, C. White, S. Reynolds, T. D'Arcy, J. J. O'Leary and F. M. Lyng, Raman spectroscopy of liquid-based cervical smear samples as a triage to stratify women who are HPV-positive on screening, *Cancers*, 2021, **13**(9), 2008, DOI: 10.3390/cancers13092008.

54 D. Traynor, I. Behl, D. O'Dea, F. Bonnier, S. Nicholson, F. O'Connell, *et al.*, Raman spectral cytopathology for cancer diagnostic applications, *Nat. Protoc.*, 2021, **16**(7), 3716–3735, DOI: 10.1038/s41596-021-00559-5.

55 K. O'Dwyer, K. Domijan, A. Dignam, M. Butler and B. M. Hennelly, Automated Raman micro-spectroscopy of epithelial cell nuclei for high-throughput classification, *Cancers*, 2021, **13**, 19, DOI: 10.3390/cancers13194767.

56 R. Muddiman and B. Hennelly, Broadband CARS high-throughput single-cell imaging, *EPJ Web Conf.*, 2023, **287**, 03018, DOI: 10.1051/epjconf/202328703018.

57 J. R. Hands, K. M. Dorling, P. Abel, K. M. Ashton, A. Brodbelt, C. Davis, *et al.*, Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) spectral discrimination of brain tumour severity from serum samples, *J. Biophotonics*, 2014, **7**(3–4), 189–199, DOI: 10.1002/jbio.201300149.

58 J. R. Hands, G. Clemens, R. Stables, K. Ashton, A. Brodbelt, C. Davis, *et al.*, Brain tumour differentiation: rapid stratified serum diagnostics via attenuated total reflection Fourier-transform infrared spectroscopy, *J. Neurooncol.*, 2016, **127**(3), 463, DOI: 10.1007/s11060-016-2060-x.

59 Technology | Dxcover. Available from: https://www.dxcover.com/technology [cited 2022 Aug 26].

60 CanSense – Innovation in cancer diagnostics. Available from: https://cansenseltd.com/ [cited 2022 Aug 26].

61 S. Roy, D. Perez-Guaita, D. W. Andrew, J. S. Richards, D. McNaughton, P. Heraud and B. R. Wood, Simultaneous ATR-FTIR Based Determination of Malaria Parasitemia, Glucose and Urea in Whole Blood Dried onto a Glass Slide, *Anal. Chem.*, 2017, **89**(10), 5238–5245, DOI: 10.1021/acs.analchem.6b04578.

62 P. Heraud, P. Chatchawal, M. Wongwattanakul, P. Tippayawat, C. Doerig, P. Jearanaikoon, D. Perez-Guaita and B. R. Wood, Infrared spectroscopy coupled to cloud-based data management as a tool to diagnose malaria: A pilot study in a malaria-endemic country, *Malar. J.*, 2019, **18**(1), 348, DOI: 10.1186/s12936-019-2945-1.

63 M. Martin, D. Perez-Guaita, D. W. Andrew, J. S. Richards, B. R. Wood and P. Heraud, The effect of common anticoagulants in detection and quantification of malaria parasitemia in human red blood cells by ATR-FTIR spectroscopy, *Analyst*, 2017, **142**(8), 1192–1199, DOI: 10.1039/C6AN02075E.

64 B. R. Wood, J. A. Adegoke, T. Chakkumpulakkal, P. Veettil, A. Dodla, K. Dias, *et al.*, Illuminating Malaria: Spectroscopy's Vital Role in Diagnosis and Research, *Spectrosc. J.*, 2024, **2**(4), 216–263, DOI: 10.3390/spectroscj2040015.

65 E. Efeoglu, M. A. Maher, A. Casey and H. J. Byrne, Toxicological assessment of nanomaterials: the role of in vitro Raman microspectroscopic analysis, *Anal. Bioanal. Chem.*, 2018, **410**(6), 1631–1646, DOI: 10.1007/s00216-017-0812-x.

66 H. J. Byrne, F. Bonnier, E. Efeoglu, C. Moore and J. McIntyre, In vitro Label Free Raman Microspectroscopic Analysis to Monitor the Uptake, Fate and Impacts of Nanoparticle Based Materials, *Front. Bioeng. Biotechnol.*, 2020, **8**, 544311, DOI: 10.3389/fbioe.2020.544311.

67 L. E. Jamieson and H. J. Byrne, Vibrational spectroscopy as a tool for studying drug-cell interaction: Could high throughput vibrational spectroscopic screening improve drug development?, *Vib. Spectrosc.*, 2017, **91**, 16–30, DOI: 10.1016/j.vibspec.2016.09.003.

68 E. Szafraniec, K. Majzner, Z. Farhane, H. J. Byrne, M. Lukawska, I. Oszczapowicz, S. Chlopicki and M. Baranska, Spectroscopic studies of anthracyclines: Structural characterization and in vitro tracking, *Spectrochim. Acta, Part A*, 2016, **169**, 152–160, DOI: 10.1016/j.saa.2016.06.035.

69 Z. Farhane, H. Nawaz, F. Bonnier and H. J. Byrne, In vitro label-free screening of chemotherapeutic drugs using Raman microspectroscopy: Towards a new paradigm of spectralomics, *J. Biophotonics*, 2018, **11**(3), e201700258, DOI: 10.1002/jbio.201700258.

70 U. Lopez-Gonzalez, A. Casey and H. J. Byrne, Monitoring the biochemical changes occurring to human keratinocytes exposed to solar radiation by Raman spectroscopy, *J. Biophotonics*, 2021, **14**(2), e202000337, DOI: 10.1002/jbio.202000337.

71 A. D. Meade, O. Howe, V. Unterreiner, G. D. Sockalingum, H. J. Byrne and F. M. Lyng, Vibrational spectroscopy in sensing radiobiological effects: Analyses of targeted and

non-targeted effects in human keratinocytes, *Faraday Discuss.*, 2016, **187**, 213–234, DOI: 10.1039/C5FD00208G.

72 J. F. Monaghan, H. J. Byrne, F. M. Lyng, A. D. Meade, J. F. Monaghan, H. J. Byrne, *et al.*, Radiobiological Applications of Vibrational Spectroscopy: A Review of Analyses of Ionising Radiation Effects in Biology and Medicine, *Radiation*, 2024, **4**(3), 276–308, DOI: 10.3390/radiation4030022.

73 F. Ravera, E. Efeoglu and H. J. Byrne, Vibrational spectroscopy for in vitro monitoring stem cell differentiation, *Molecules*, 2020, **25**, 5554, DOI: 10.3390/molecules25235554.

74 I. Chaudhary, N. Jackson, D. Denning, L. O'Neill and H. J. Byrne, Contributions of vibrational spectroscopy to virology: A review, *Clin. Spectrosc.*, 2022, **4**, 100022, DOI: 10.1016/j.clispe.2022.100022.

75 V. Notarstefano, S. Sabbatini, C. Pro, A. Belloni, G. Orilisi, C. Rubini, H. J. Byrne, L. Vaccari and E. Giorgini, Exploiting fourier transform infrared and Raman microspectroscopies on cancer stem cells from oral squamous cells carcinoma: New evidence of acquired cisplatin chemoresistance, *Analyst*, 2020, **145**(24), 8038–8049, DOI: 10.1039/D0AN01623C.

76 D. Perez-Guaita, G. Quintas, Z. Farhane, R. Tauler and H. J. Byrne, Data mining Raman microspectroscopic responses of cells to drugs in vitro using multivariate curve resolution-alternating least squares, *Talanta*, 2020, **208**, 120386, DOI: 10.1016/j.talanta.2019.120386.

77 D. Pérez-Guaita, G. Quintás, Z. Farhane, R. Tauler and H. J. Byrne, Combining Pharmacokinetics and Vibrational Spectroscopy: MCR-ALS Hard-and-Soft Modelling of Drug Uptake In Vitro Using Tailored Kinetic Constraints, *Cells*, 2022, **11**(9), 1555, DOI: 10.3390/cells11091555.

78 D. Perez-Guaita, G. Quintas, Z. Farhane, R. Tauler and H. J. Byrne, Corrigendum: "Data mining Raman microspectroscopic responses of cells to drugs in vitro using multivariate curve resolution-alternating least squares" [Talanta 208 (2020) 120386], *Talanta*, 2022, **236**, 122682, DOI: 10.1016/j.talanta.2021.122682.

79 N. Patil, O. Howe, P. Cahill and H. J. Byrne, Monitoring and modelling the dynamics of the cellular glycolysis pathway: A review and future perspectives, *Mol. Metab.*, 2022, **66**, 101635, DOI: 10.1016/j.molmet.2022.101635.

80 Z. Mirveis, O. Howe, P. Cahill, N. Patil and H. J. Byrne, Monitoring and modelling the glutamine metabolic pathway: a review and future perspectives, *Metabolomics*, 2023, **19**(8), 1–24, DOI: 10.1007/s11306-023-02031-9.

81 H. J. Byrne, Spectralomics – Towards a holistic adaptation of label free spectroscopy, *Vib. Spectrosc.*, 2024, **132**, 103671, DOI: 10.1016/j.vibspec.2024.103671.

82 A. A. Makki, V. Massot, H. J. Byrne, R. Respaud, D. Bertrand, E. Mohammed, I. Chourpa and F. Bonnier, Vibrational spectroscopy for discrimination and quantification of clinical chemotherapeutic preparations, *Vib. Spectrosc.*, 2021, **113**, 103200, DOI: 10.1016/j.vibspec.2020.103200.

83 A. A. Makki, V. Massot, H. J. Byrne, R. Respaud, D. Bertrand, E. Mohammed, I. Chourpa and F. Bonnier, Understanding the discrimination and quantification of monoclonal antibodies preparations using Raman spectroscopy, *J. Pharm. Biomed. Anal.*, 2021, **194**, 113734, DOI: 10.1016/j.jpba.2020.113734.

84 A. A. Makki, F. Bonnier, R. Respaud, F. Chtara, A. Tfayli, C. Tauber, D. Bertrand, H. J. Byrne, E. Mohammed and I. Chourpa, Qualitative and quantitative analysis of therapeutic solutions using Raman and infrared spectroscopy, *Spectrochim. Acta, Part A*, 2019, **218**, 97–108, DOI: 10.1016/j.saa.2019.03.056.

85 A. A. Makki, S. Elderderi, V. Massot, R. Respaud, H. J. Byrne, C. Tauber, D. Bertrand, E. Mohammed, I. Chourpa and F. Bonnier, In situ Analytical Quality Control of chemotherapeutic solutions in infusion bags by Raman spectroscopy, *Talanta*, 2021, **228**, 122137, DOI: 10.1016/j.talanta.2021.122137.

86 E. Szczesny-Malysiak, J. Dybas, A. Blat, K. Bulat, K. Kus, M. Kaczmarska, A. Wajda, K. Malek, S. Chlopicki and K. M. Marzec, Irreversible alterations in the hemoglobin structure affect oxygen binding in human packed red blood cells, *Biochim. Biophys. Acta, Mol. Cell Res.*, 2020, **1867**(11), 118803, DOI: 10.1016/j.bbamcr.2020.118803.

87 J. Dybas, A. Wajda, F. C. Alcicek, M. Kaczmarska, K. Bulat, E. Szczesny-Malysiak, *et al.*, Label-free testing strategy to evaluate packed red blood cell quality before transfusion to leukemia patients, *Sci. Rep.*, 2022, **12**(1), 21849, DOI: 10.1038/s41598-022-26309-5.

88 E. L. Izake, Forensic and homeland security applications of modern portable Raman spectroscopy, *Forensic Sci. Int.*, 2010, **202**(1–3), 1–8, DOI: 10.1016/j.forsciint.2010.03.020.

89 P. Raghavendra and T. Pullaiah, Cellular and Molecular Diagnostics, in *Advances in Cell and Molecular Diagnostics*, 2018, pp. 1–32.

90 D. Müller, D. Schuhmacher, S. Schörner, F. Großerueschkamp, I. Tischoff, A. Tannapfel, *et al.*, Dimensionality reduction for deep learning in infrared microscopy: a comparative computational survey, *Analyst*, 2023, **148**(20), 5022–5032, DOI: 10.1039/D3AN00166K.

91 C. A. Meza Ramirez, M. Greenop, L. Ashton and I. ur Rehman, Applications of machine learning in spectroscopy, *Appl. Spectrosc. Rev.*, 2021, **56**(8–10), 733–763, DOI: 10.1080/05704928.2020.1859525.

92 Regulation-EU-2024/1689-EN-EUR-Lex. Available from: https://eur-lex.europa.eu/eli/reg/2024/1689/oj/eng [cited 2025 Jun 7].

93 N. Goertzen, R. Pappesch, J. Fassunke, T. Brüning, Y. D. Ko, J. Schmidt, *et al.*, Quantum Cascade Laser-Based Infrared Imaging as a Label-Free and Automated Approach to Determine Mutations in Lung Adenocarcinoma, *Am. J. Pathol.*, 2021, **191**(7), 1269–1280, DOI: 10.1016/j.ajpath.2021.04.013.

94 S. Tiwari, T. Triulzi, S. Holton, V. Regondi, B. Paolini, E. Tagliabue, *et al.*, Infrared Spectroscopic Imaging Visualizes a Prognostic Extracellular Matrix-Related

Signature in Breast Cancer, *Sci. Rep.*, 2020, **10**(1), 5442, DOI: 10.1038/s41598-020-62403-2.

95 A. Zetterström, N. P. Lockyer and P. Gardner, Multimodal imaging of tissue using the combination of vibrational spectroscopy and mass spectrometry, *Appl. Spectrosc. Rev.*, 2025, 1–25, DOI: 10.1080/05704928.2025.2488469.

96 J. H. Rabe, D. A. Sammour, S. Schulz, B. Munteanu, M. Ott, K. Ochs, *et al.*, Fourier Transform Infrared Microscopy Enables Guidance of Automated Mass Spectrometry Imaging to Predefined Tissue Morphologies, *Sci. Rep.*, 2018, **8**, 313, DOI: 10.1038/s41598-017-18477-6.

97 E. Gazi, N. P. Lockyer, J. C. Vickerman, P. Gardner, J. Dwyer, C. A. Hart, *et al.*, Imaging ToF-SIMS and synchrotron-based FT-IR microspectroscopic studies of prostate cancer cell lines, *Appl. Surf. Sci.*, 2004, **231–232**, 452–456, DOI: 10.1016/j.apsusc.2004.03.170.

98 K. E. Witzke, F. Großerueschkamp, H. Jütte, M. Horn, F. Roghmann, N. von Landenberg, *et al.*, Integrated Fourier Transform Infrared Imaging and Proteomics for Identification of a Candidate Histochemical Biomarker in Bladder Cancer, *Am. J. Pathol.*, 2019, **189**(3), 619–631, DOI: 10.1016/j.ajpath.2018.11.018.

99 N. Goffin, E. Buache, C. Charpentier, V. Lehrter, H. Morjani, C. Gobinet, *et al.*, Trajectory Inference for Unraveling Dynamic Biological Processes from Raman Spectral Data, *Anal. Chem.*, 2023, **95**(9), 4395–4403, DOI: 10.1021/acs.analchem.2c04901.

100 K. J. Kobayashi-Kirschvink, C. S. Comiter, S. Gaddam, T. Joren, E. I. Grody, J. R. Ounadjela, *et al.*, Prediction of single-cell RNA expression profiles in live cells by Raman microscopy with Raman2RNA, *Nat. Biotechnol.*, 2024, 1–9, DOI: 10.1038/s41587-023-02082-2.

101 SpectrAI-Home. Available from: https://spectrai.org/ [cited 2024 Dec 29].

102 C. C. Horgan and M. S. Bergholt, spectrai: A deep learning framework for spectral data, *J. Spectr. Imaging.*, 2021, 11, DOI: 10.48550/arXiv.2108.07595.

103 D. Ferguson, A. Henderson, E. F. McInnes, R. Lind, J. Wildenhain and P. Gardner, Infrared micro-spectroscopy coupled with multivariate and machine learning techniques for cancer classification in tissue: a comparison of classification method, performance, and pre-processing technique, *Analyst*, 2022, **147**(16), 3709–3722, DOI: 10.1039/D2AN00775D.

104 D. Perez-Guaita, K. Chrabaszcz, K. Malek and H. J. Byrne, Multimodal vibrational studies of drug uptake in vitro: Is the whole greater than the sum of their parts?, *J. Biophotonics*, 2020, **13**(12), e202000264, DOI: 10.1002/jbio.202000264.

105 I. Behl, G. Calado, A. Vishwakarma, D. Traynor, S. Flint, S. Galvin, *et al.*, Identification of High-Risk Oral Leukoplakia (Olk) Using Combined Raman Spectroscopic Analysis of Brush Biopsy and Saliva Samples: A Proof of Concept Study, *Spectrochim. Acta, Part A*, 2025, **330**, 125721, DOI: 10.1016/j.saa.2025.125721.

106 H. J. Koster, A. Guillen-Perez, J. S. Gomez-Diaz, M. Navas-Moreno, A. C. Birkeland and R. P. Carney, Fused Raman spectroscopic analysis of blood and saliva delivers high accuracy for head and neck cancer diagnostics, *Sci. Rep.*, 2022, **12**(1), 18464, DOI: 10.1038/s41598-022-22197-x.

107 Zenodo. Available from: https://zenodo.org/communities/clirspec/about [cited 2025 Jan 25].

108 GO FAIR initiative: Make your data & services FAIR. Available from: https://www.go-fair.org/ [cited 2025 Jan 25].

109 FAIRSpectra. Available from: https://fairspectra.net/ [cited 2025 Jan 25].

110 STELLARIS CRS Coherent Raman Scattering Microscope | Products | Leica Microsystems. Available from: https://www.leica-microsystems.com/products/confocal-microscopes/p/stellaris-8-crs/ [cited 2025 Jan 25].

111 Technology – CRI Chemometric imaging. Available from: https://www.cambridgeramanimaging.com/technology/ [cited 2025 Jan 25].

112 Best-In-Class Mid-Infrared, Quantum Cascade Laser Provider | DRS Daylight Solutions. Available from: https://www.daylightsolutions.com/ [cited 2025 Jan 25].

113 D. Ferguson, N. Kroeger-Lui, D. Dreisbach, C. A. Hart, D. F. Sanchez, P. Oliveira, *et al.*, Full fingerprint hyperspectral imaging of prostate cancer tissue microarrays within clinical timeframes using quantum cascade laser microscopy, *Analyst*, 2025, **150**, 1741–1753, DOI: 10.1039/D5AN00046G.

114 nano-FTIR. Available from: https://www.attocube.com/en/products/microscopes/nanoscale-imaging-spectroscopy/technology/nano-FTIR [cited 2025 Jan 25].

115 AFM-IR: Technology and Applications in Nanoscale Infrared Spectroscopy and Chemical Imaging | Bruker. Available from: https://www.bruker.com/en/products-and-solutions/infrared-and-raman/nanoscale-infrared-spectrometers/nanoir-publications/afm-ir-technology-and-applications-in-nanoscale-infrared-spectr.html [cited 2025 Jan 25].

116 Fluorescence guided sub-500 nm IR & simultaneous Raman spectroscopy. Available from: https://www.photothermal.com/products/mlrage-ls/ [cited 2025 Jan 25].

117 RiverD International B.V. Available from: https://www.riverd.com/ [cited 2024 Dec 29].

118 InSplorer Endoscope – Lightcore Technologies. Available from: https://lightcore.tech/flexible-endoscopes-m-fip/ [cited 2022 Aug 26].

119 Invenio Imaging Announces First Patients Enrolled in US Pivotal Study of AI-Based Image Analysis Module for Lung Cancer. Available from: https://www.prnewswire.com/news-releases/invenio-imaging-announces-first-patients-enrolled-in-us-pivotal-study-of-ai-based-image-analysis-module-for-lung-cancer-302218302.html?sp_sn=linkedin&spclid=70AD40BB-D24D-4605-B814-5D2BD86BBF36 [cited 2024 Dec 29].

120 J. Cameron, M. Baker, G. Antoniou, P. Brennan, H. Butler, D. Eustace, *et al.*, BIOM-10. clinical performance evaluation of a brain cancer liquid biopsy, *Neurooncology*, 2024,

26(Supplement_8), viii20–viii21, DOI: **10.1093/neuonc/noae165.0083**.

121 H. Butler, M. Baker, M. Hegarty, D. Finlayson, K. Hollinshead, H. Munford, *et al.*, A spectroscopic serum based blood test for brain tumours: Optimisation for high-throughput sampling and the health economic impacts, *Neurooncology*, 2018, **20**(suppl_1), i4, DOI: **10.1093/neuonc/nox237.015**.

122 C. Hughes and M. J. Baker, Can mid-infrared biomedical spectroscopy of cells, fluids and tissue aid improvements in cancer survival? A patient paradigm, *Analyst*, 2016, **141**(2), 467–475, DOI: **10.1039/C5AN01858G**.

123 ResearchGate. Available from: **https://www.researchgate.net/profile/Josep-Sule-Suso/research** [cited 2024 Dec 29].

124 ResearchGate. Available from: **https://www.researchgate.net/profile/Senada-Koljenovic/research** [cited 2024 Dec 29].

125 ResearchGate. Available from: **https://www.researchgate.net/profile/Hugh-Barr/research** [cited 2024 Dec 29].

126 Digital pathology to improve cancer screening and save lives – GOV.UK. Available from: **https://www.gov.uk/government/news/digital-pathology-to-improve-cancer-screening-and-save-lives** [cited 2025 Jan 25].

127 National Pathology Imaging Co-operative (NPIC) | UKHDRA. Available from: **https://ukhealthdata.org/members/npic/** [cited 2025 Jan 25].

128 Home – PathLAKE: PathLAKE. Available from:**https://www.pathlake.org/** [cited 2025 Jan 25].